

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of the Claims:

1-7. (Canceled)

8. (Currently Amended) A method for treating an inflammatory disease in a mammal ~~comprising responsive cells~~, said method comprising administering to a mammal in need thereof a pharmaceutical composition comprising a prophylactically or therapeutically effective amount of a chemically modified erythropoietin and an anti-inflammatory agent or a prophylactically or therapeutically effective amount of a chemically modified erythropoietin and an immunomodulatory agent,

wherein said inflammatory disease is stroke,

wherein said chemically modified erythropoietin has a reduced level of in vivo erythropoietic activity compared to native erythropoietin as determined by the exhypoxic polycythemic mouse bioassay, and has tissue protective activity in vivo as determined by the middle cerebral artery occlusion test,

and wherein said chemically modified erythropoietin comprises:

- i) a chemically modified arginine residue at position 31, 37, 41, 80, 103, 130, 137, 158, 166, 170, 177, 189, or 193 of SEQ ID NO:5;
- ii) a chemically modified lysine residue at position 47, 72, 79, 124, 143, 167, 179, or 181 of SEQ ID NO:5 or a chemical modified N-terminal amino group;
- iii) a chemically modified tyrosine residue at position 42, 76, 172, or 183 of SEQ ID NO:5;
- iv) a chemically modified aspartic acid or a glutamic acid residue at position 35, 70, 123, 150, 163, 192, 40, 45, 48, 50, 58, 64, 82, 89, 99, 116, 144, or 186 of SEQ ID NO:5; and

v) a chemically modified tryptophan residue at position 78, 91, or 115 of SEQ ID NO:5,

wherein the chemical modification results from one of the following chemical reactions: acetylation; carbamylation; succinylation; carboxymethyllysination; alkylation; nitration; iodination; biotinylation; a reaction with n-bromosuccinimide, chlorosuccinimide, vicinal diketone, or glyoxal; a reaction with R-glyoxal, wherein R is selected from the group consisting of aryl, heteroaryl, lower alkyl, lower alkoxy, cycloalkyl group, and alpha-deoxyglycitolyl; or a reaction with carbodiimide followed by reaction with an amine.

9. (Previously Amended) The method of claim 8, wherein the anti-inflammatory agent is selected from the group consisting of a steroid, a non-steroidal anti-inflammatory drug, a beta-agonist, an anticholinergic agent, a methyl xanthine, gold injection, a sulphasalazine, penicillamine, an anti-angiogenic agent, dapsone, psoralen, an anti-malarial agent, an anti-viral agent, and an antibiotic.

10. (Original) The method of claim 8, wherein the immunomodulatory agent is selected from the group consisting of a proteinaceous agent, a peptide mimetic, an antibody, a nucleic acid molecule, a small molecule, an organic compound, an inorganic compound, methothrexate, leflunomide, cyclophosphamide, cytoxan, Immuran, cyclosporine A, minocycline, azathioprine, an antibiotic, methylprednisolone (MP), a corticosteroid, a steroid, mycophenolate mofetil, rapamycin, mizoribine, deoxyspergualin, brequinar, a malononitriloamidine, a T cell receptor modulator, and a cytokine receptor modulator.

11. (Canceled)

12. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin is asialoerythropoietin or phenylglyoxal-erythropoietin.

13-23. (Canceled)

24. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin is an erythropoietin comprising a R-glyoxal moiety on the one or more arginine residues, wherein R is aryl or alkyl moiety.

25. (Currently Amended) The method of claim 24, wherein said chemically

modified erythropoietin is phenylglyoxal-erythropoietin.

26. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin is an erythropoietin in which at least one arginine residue is modified by reaction with a vicinal diketone selected from the group consisting of 2,3-butanedione and cyclohexanedione.

27. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin is an erythropoietin in which at least one arginine residue is reacted with 3-deoxyglucosone.

28. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin is an erythropoietin molecule comprising at least one biotinylated lysine or biotinylated N-terminal amino group.

29. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin molecule is biotinylated.

30. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin is a glucitolyl lysine erythropoietin or a fructosyl lysine erythropoietin.

31. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin is an erythropoietin having at least one carbamylated lysine residue.

32. (Original) The method of claim 31, wherein said carbamylated erythropoietin is selected from the group consisting of alpha-N-carbamoylerythropoietin; N-epsilon-carbamoylerythropoietin; alpha-N-carbamoyl, N-epsilon-carbamoylerythropoietin; alpha-N-carbamoylasialoerythropoietin; N-epsilon-carbamoylasialoerythropoietin; alpha-N-carbamoyl, N-epsilon-carbamoylasialoerythropoietin; alpha-N-carbamoylhyposialoerythropoietin; N-epsilon-carbamoylhyposialoerythropoietin; and alpha-N-carbamoyl, N-epsilon-carbamoylhyposialoerythropoietin.

33. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin is an erythropoietin in which at least one lysine residue is acylated.

34. (Currently Amended) The method of claim 33, wherein a lysine residue of said chemically modified erythropoietin is acetylated.

35. (Original) The method of claim 34, wherein said acetylated erythropoietin is selected from the group consisting of alpha-N-acetylerythropoietin; N-epsilon-acetylerythropoietin; alpha-N-acetyl, N-epsilon-acetylerythropoietin; alpha-N-acetylasialoerythropoietin; N-epsilon-acetylasialoerythropoietin; alpha-N-acetyl, N-epsilon-acetylasialoerythropoietin; alpha-N-acetylhyposialoerythropoietin; N-epsilon-acetylhyposialoerythropoietin; and alpha-N-acetyl, N-epsilon-acetylhyposialoerythropoietin.

36. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin is an erythropoietin comprising a succinylated lysine residue.

37. (Currently Amended) The method of claim 36, where said succinylated erythropoietin is selected from the group consisting of alpha-N-succinylerythropoietin; N-epsilon-succinylerythropoietin; alpha-N-succinyl, N-epsilon-succinylerythropoietin; alpha-N-succinylasialoerythropoietin; N-epsilon-succinylasialoerythropoietin; alpha-N-succinyl, N-epsilon-succinylasialoerythropoietin; alpha-N-succinylhyposialoerythropoietin; N-epsilon-succinylhyposialoerythropoietin; and alpha-N-succinyl, N-epsilon-succinylhyposialoerythropoietin.

38. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin is an erythropoietin with at least one lysine residue modified by a 2, 4, 6-trinitrobenzenesulfonic acid salt.

39. (Previously Amended) The method of claim 38, wherein the salt is 2, 4, 6-trinitrobenzenesulfonate sodium.

40. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin is an erythropoietin in which at least one tyrosine residue is nitrated and/or iodinated.

41. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin is an erythropoietin in which an aspartic acid and/or glutamic acid residue is reacted with a carbodiimide followed by reaction with an amine.

42. (Original) The method of claim 41, wherein said amine is glycnamide.

43-52. (Canceled)

53. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin is an alpha-N-carbamoyl, N-epsilon-carbamoylerythropoietin.

54. (Currently Amended) The method of claim 8, wherein said chemically modified erythropoietin is non-erythropoietic.

55. (Currently Amended) The method of claim 8, wherein [[the]] said chemically modified erythropoietin and the anti-inflammatory agent or immunomodulatory agent are administered to the mammal concurrently.

56. (Currently Amended) A method for treating an inflammatory disease in a mammal comprising administering to a mammal in need thereof a prophylactically or therapeutically effective amount of a chemically modified erythropoietin,

wherein said inflammatory disease is stroke,

wherein said chemically modified erythropoietin has a reduced level of in vivo erythropoietic activity compared to native erythropoietin as determined by the exhypoxic polycythemic mouse bioassay, and has tissue protective activity in vivo as determined by the middle cerebral artery occlusion test,

and wherein said chemically modified erythropoietin comprises:

- i) a chemically modified arginine residue at position 31, 37, 41, 80, 103, 130, 137, 158, 166, 170, 177, 189, or 193 of SEQ ID NO:5;
- ii) a chemically modified lysine residue at position 47, 72, 79, 124, 143, 167, 179, or 181 of SEQ ID NO:5 or a chemically modified N-terminal amino group;
- iii) a chemically modified tyrosine residue at position 42, 76, 172, or 183 of SEQ ID NO:5;
- iv) a chemically modified aspartic acid residue at position 35, 70, 123, 150, 163, or 192 of SEQ ID NO:5;
- v) a chemically modified glutamic acid residue at position 40, 45, 48, 50, 58, 64, 82, 89, 99, 116, 144, or 186 of SEQ ID NO:5; or

vi) a chemically modified tryptophan residue at position 78, 91, or 115 of SEQ ID NO:5,

wherein the chemical modification results from one of the following chemical reactions: acetylation; carbamylation; succinylation; carboxymethyllysination; alkylation; nitration; iodination; biotinylation; a reaction with n-bromosuccinimide, chlorosuccinimide, vicinal diketone, or glyoxal; a reaction with R-glyoxal wherein R is selected from the group consisting of aryl, heteroaryl, lower alkyl, lower alkoxy, cycloalkyl group, and alpha-deoxyglycitolyl; or a reaction with carbodiimide followed by reaction with an amine.

57. (Currently Amended) The method of claim 56, wherein said chemically modified erythropoietin is an erythropoietin having at least one carbamylated lysine residue.

58. (Previously Presented) The method of claim 57, wherein said carbamylated erythropoietin is selected from the group consisting of alpha-N-carbamoylerythropoietin; N-epsilon-carbamoylerythropoietin; alpha-N-carbamoyl, N-epsilon-carbamoylerythropoietin; alpha-N-carbamoylasialoerythropoietin; N-epsilon-carbamoylasialoerythropoietin; alpha-N-carbamoyl, N-epsilon-carbamoylasialoerythropoietin; alpha-N-carbamoylhyposialoerythropoietin; N-epsilon-carbamoylhyposialoerythropoietin; and alpha-N-carbamoyl, N-epsilon-carbamoylhyposialoerythropoietin.

59. (Currently Amended) The method of claim 56, wherein said chemically modified erythropoietin is non-erythropoietic.

60. (New) The method of claim 58, wherein said chemically modified erythropoietin is an alpha-N-carbamoyl, N-epsilon-carbamoylerythropoietin.